with conservative management in these patients. Thus, it appears that most patients receiving thrombolytic therapy can be successfully managed without the need for routine coronary angioplasty unless they have symptoms or objective evidence of recurrent ischemia.

At this time there are no definitive data that would show the superiority of one thrombolytic agent over another in terms of improving survival or left ventricular function in patients with acute myocardial infarction. Although the TIMI phase I trial showed that, compared with streptokinase therapy, administering intravenous tissue plasminogen activator achieved a higher incidence of coronary artery patency 90 minutes after it was started, a New Zealand trial failed to show that giving tissue plasminogen activator was better than administering streptokinase in improving overall left ventricular function. It should be noted that both of these trials involved relatively small numbers of patients. Currently there are several large ongoing studies comparing the relative benefit of various thrombolytic agents on survival.

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Reducing Morbidity and Mortality Due to Asthma

DESPITE MAJOR ADVANCES in the understanding of its pathogenesis and the availability of a large number of drugs, morbidity and mortality due to asthma appear to be on the rise. Although the reasons for this disturbing paradox are unclear, there are certain broad treatment guidelines that, if diligently followed, will help to reduce the growing menace of asthma.

Although patients of any age, sex, and race can die of asthma, the disease more frequently ravages socioeconomically handicapped members of the society. In the United States blacks have a higher incidence of death from asthma than whites. Adults older than 65 years and children between the ages of 10 and 14 years are particularly susceptible. Persons with specific immunoglobulin E antibodies to common inhalant allergens are at an increased risk for acute severe attacks of asthma. Most of the patients who die of asthma have a history of severe, poorly controlled disease with poor compliance. Many of these patients also have emotional ailments, particularly depression, isolation, and problems of self-image.

Physicians often fail to realize that there is generally a poor correlation between the symptoms of asthma and the degree of airway obstruction. Patients, on the other hand, commonly develop a tolerance to their symptoms. Thus, there is a failure on the part of both physician and patient to appreciate the severity of bronchial narrowing. Educating patients about recognizing important symptoms and emphasizing the necessity of monitoring airway obstruction by peak flow measurements are the basic steps towards controlling asthma. More often than not, patients can be persuaded to buy a flow meter. Physicians who take care of asthma patients should not only have a peak flow meter on their desk but should also have easy access to a pulmonary function laboratory.

One of the problems related to asthma therapy lies in the way the treatment is delivered to the airways. Although the inhaled route is an effective way of delivering bronchodilators, surveys have shown that more than 50% of patients prescribed an aerosol inhaler used it incorrectly. Furthermore, other studies have revealed that physicians often do a less than satisfactory job of instructing their patients on how to use inhalers. The problem of poor coordination can now be corrected by using spacers and newly developed breath-actuated inhalers. These devices are of particular help in very young and elderly patients who find it hard to use metered-dose inhalers.

Although the treatment of asthma should be tailored to the needs of individual patients, inhaled selective β_2-adrenergic agents constitute the first line of therapy in chronic asthma. When a properly administered β_2-adrenergic drug—including the use of spacers and breath-actuated inhalers—does not provide effective relief of bronchospasm, aerosolized corticosteroids should be prescribed to suppress the airway inflammation that appears to underlie the severe bronchial hyperreactivity of asthma. If used effectively, this combination not only produces maximum improvement in peak flow rates but also cuts down the need for parenteral steroids. Patients who do not respond to the β_2-adrenergic drugs and aerosolized corticosteroids combination deserve a trial of cromolyn sodium. This prophylactic agent is particularly useful for young patients with asthma who are known to have allergies and exercise-induced asthma. Recent studies have found that cromolyn sodium reduces bronchial hyperreactivity in adult patients with asthma as well.

In summary, the rising tide of morbidity and death in asthma can be countered by recognizing high-risk patients, by accurately assessing the severity of airway obstruction, by properly delivering bronchodilators in the airway, and by prescribing cromolyn sodium and corticosteroids judiciously.

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Treatment of Small-Cell Lung Cancer

MANY COMBINATION chemotherapy regimens have activity in patients with small-cell lung cancer. In contrast to the treatment of non-small-cell lung cancer, surgical excision is not generally recommended for patients with small-cell lung cancer because of the propensity for distant spread of the

disease—even if it is not apparent on the initial clinical evaluation—and the excellent initial response to chemotherapy. Patients with both limited stage (disease present only in one side of the thorax and regional lymph nodes) and extensive stage (disease spread beyond the confines of limited disease) small-cell lung cancer have an excellent chance of responding to chemotherapy. Using standard regimens patients with limited disease have a 50% complete remission rate, and approximately 20% of patients with extensive disease will attain a complete remission. A complete remission implies total resolution of all clinical signs and symptoms and radiographic evidence of malignancy. Patients with small-cell lung cancer who achieve a complete remission have an improved quality of life and median survival. Unfortunately, recurrences frequently develop, and the median survivals for patients with limited disease and those with extensive disease are only 12 and 8 months, respectively.

The two most common combination chemotherapy regimens used in the United States for patients with small-cell lung cancer are vincristine sulfate, doxorubicin (Adriamycin) hydrochloride, and cyclophosphamide (VAC) and etoposide and cisplatin. In the past two years, four prospectively randomized clinical trials that tested combinations of these drugs alone and in conjunction with consolidative chest radiotherapy have been reported.

In 1987 the Cancer and Leukemia Group B reported the experience in 399 patients with limited disease who were randomly assigned to receive initial chemotherapy—vincristine, Adriamycin, cyclophosphamide, and etoposide—combined with chest radiotherapy versus delayed chest radiotherapy sandwiched between cycles of chemotherapy versus chemotherapy only. The complete remission rate and median survival were best in the group receiving combined methods. For initial chemotherapy combined with chest radiotherapy, the complete remission rate was 49% and median survival 13.4 months; for chemotherapy plus delayed radiotherapy, the complete remission rate was 58% and median survival 12.0 months; and for chemotherapy alone, the complete remission rate was 36% and the median survival 10.5 months. Disease-free survival was prolonged three to four months for the combined treatment methods.

Two studies were reported from the National Cancer Institute of Canada. In the first, 289 patients with extensive disease were randomly assigned to receive six cycles of VAC or six total cycles of VAC alternating each cycle with etoposide and cisplatin. Patients treated with the alternating regimen had a slightly increased complete remission rate (13% versus 10%) and prolonged median survival (9.6 months versus 8 months). No significant difference in overall survival was detected ($P = .4$).

The second study from the National Cancer Institute of Canada was undertaken in 300 patients with limited disease. Patients were randomly assigned to receive VAC alternating with etoposide and cisplatin for a total of six cycles, or three cycles of VAC followed by three cycles of etoposide and cisplatin. Again, the alternating regimen resulted in a slight but not significantly different increase in complete remission rate (52% versus 44%) and median survival (15.4 months versus 14.9 months).

In 1988 the Southeastern Cancer Study Group reported the experience in 148 patients with limited disease who were randomly assigned to receive six cycles of VAC or six cycles of VAC followed by two cycles of etoposide and cisplatin as consolidation therapy. Only responding patients were given consolidation therapy. The complete remission rates were similar in both groups (64% versus 65%), but the patients who received consolidation therapy had a significantly prolonged median survival (24.4 months versus 17 months, $P = .0094$).

In summary, a regimen of VAC alternating with etoposide and cisplatin was associated with a slight improvement in the complete remission rate and median survival, but the differences were generally small and of minimal clinical significance.

With current therapies, most patients with small-cell lung cancer continue to die of recurrent drug-resistant disease. Active basic and clinical research is underway to evaluate the mechanisms and means of reversing drug resistance in these patients. Because the chance of cure using any standard treatment method is extremely small, all eligible patients with this disease should continue to be enrolled in appropriately designed clinical trials.

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